REMARKS

Applicant has submitted herewith an updated supplemental information disclosure statement that corrects any errors in the previously filed information disclosure statement. This information disclosure statement is proper and timely pursuant to 37 CFR § 1.97(b)(4), in that it is being filed before the mailing of a first Office action after the filing of a request for continued examination. Those references not considered by the Examiner in the previously filed information disclosure statement are listed and properly submitted in the present information disclosure statement. Applicant respectfully requests consideration of the cited documents.

Claims 1-11, 13-15, 18, 20-26, 29, 31, 32, 36-46, 48, and 49 are pending. Claims 6, 24, and 41 have been amended to recite that the emulsifying agent is present in the aqueous phase between 0 and 10% (w/w). Support for this amendment can be found at least at paragraph [0079]. No new matter has been added by this amendment. Based on the amendment to claims 6, 24, and 41, Applicant respectfully requests withdrawal of the rejection under 35 U.S.C. § 112, 1st paragraph (new matter).

Claims 1-11, 13-15, 18, 20-26, 29, 31, 32, 36-46, 48, and 49 are rejected under 35 U.S.C. § 103(a) as being obvious over WO/2000/062761 to Vuaridel et al. ("Vuaridel"), in view of US/2001/00335352 to Ozerov ("Ozerov"), U.S. Patent 5,629,277 to Plishka ("Plishka"), and Buwalda, "Molecular Aggregation in Water: The Interplay of Hydrophobic and Electrostatic Interactiosn" University of Groningen, Doctoral Dissertation, 19 November 2001, Chapter 5, pages 97-118 ("Buwalda"). Applicant respectfully traverses this rejection.

The Examiner states that Vuaridel does not teach the anion 1-hydroxy-2-naphthoate. However, Vuaridel fails to disclose an organic ion of any kind in the aqueous phase. Rather,

Vuaridel teaches that organic ions can be used to form salts of peptides in the inner organic phase. Vuaridel at Example 1. While Vuaridel suggests adding inorganic salts, such as sodium chloride, to the aqueous phase to increase zeta potential between polymer particles, Vuaridel fails to teach or suggest adding an organic ion to the aqueous phase. Vuaridel, page 11, lines 5-9.

The Examiner relies on Plishka's disclosure of the hydrotrope 1-hydroxy-2-naphthoate, in view of Buwalda's discussion of hydrotropes and Ozerov's discussion of zeta potential, to resolve the deficiency in Vuaridel. Specifically, the Examiner argues that because hydrotropes are known to increase the solubility of sparingly soluble solutes in an aqueous phase, one of skill in the art would be motivated to use a hydrotrope, *e.g.*, 1-hydroxy-2-naphthoate, in the aqueous phase of Vuaridel. Office action at page 5. Applicant respectfully disagrees.

Hydrotropes are not disclosed in any reference as being useful for increasing the zeta potential of dispersed polymer particles in an inner organic phase. The Examiner relies on Ozerov for a disclosure indicating that increasing zeta potential of particles results in a more stable dispersion, pointing to Ozerov at paragraph [0004]:

> The stability of a particle suspended in a bulk medium is related to the zeta potential of the particle. Stable particles remain dispersed whereas unstable particles tend to agglomerate and eventually precipitate out of the solution. The higher the zeta potential, the more stable the system is since highly charged particles repel one another and remain dispersed.

Hydrotropes, however, are not disclosed as being useful for increasing the zeta potential of polymer particles in an inner organic phase. Rather, hydrotropes are disclosed as being useful for increasing the solubility of solutes in the aqueous phase. Plishka discloses that "Hydrodropes, [sic] when present in an aqueous phase at sufficient concentration, can increase the solubility of sparingly soluble solutes in the aqueous phase." Plishka at column 3, lines 9-11 (emphasis

added). Buwalda discloses that hydrotropes are known to act as solubilizing agents in drug formulations. Buwalda, page 99, last full paragraph. Hydrotropes increasing the solubility of solutes in an aqueous phase does not translate to hydrotropes increasing zeta potential of particles in an inner organic phase. The Examiner makes the unsupported conclusion that hydrotropes would have predictably increased particle repulsion of particles in the inner organic phase of Vuaridel. Office action at page 5. However, nothing in the art of record suggests this.

Vuaridel teaches away from increasing the solubility of the drug in the aqueous phase, for which hydrotropes are disclosed as useful. It follows that Vuaridel teaches away from hydrotropes in the aqueous phase. Vuaridel discloses that:

> When a solvent such as ethyl acetate is used, it has been surprisingly found that the encapsulation efficiency is increased when using cold solutions, by optimising the solubility of the solvent in water, by reducing the aqueous solubility of the drug, and by slowing down its diffusion. In other words, the present invention achieves the effect of further reducing the already small amount of diffusion of internal particle substances to the exterior.

Vuaridel at page 7, lines 14-20 (emphasis added). Encapsulation efficiency in the process of Vuaridel is therefore enhanced when the drug solubility in the aqueous phase is reduced. Hydrotropes, according to Plishka and Buwalda, increase the solubility of solutes in the aqueous phase. Hydrotropes would be expected to lower the encapsulation efficiency in the process of Vuaridel. Accordingly, Vuaridel teaches away from using hydrotropes in the aqueous phase. The combination of Vuaridel, Plishka, and Buwalda is therefore improper.

For these reasons, Applicant respectfully requests withdrawal of the rejection. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue. The Commissioner is hereby

authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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